DOCUMENT-IDENTIFIER: US 4710472 A
TITLE: Magnetic separation device

---------- KWIC ---------

DEPR:
The magnetic depletion devices are used to selectively remove cells from tissues such as blood or bone marrow containing a mixture of any cell types. The devices can be used to deplete a cell population from the tissue. Another use is to selectively concentrate a cell population in blood, marrow, or a suspension of cells from lymph nodes or spleen, to aid in detection, or in order to purify the cell sub-population. Selective depletion or enrichment of cell types with the device is accomplished using various types of immunomagnetic microspheres which selectively attach to target cells, or other objects coated with specific monoclonal antibodies. Utility may also be seen in concentrating or removing substances from a mixture.

DOCUMENT-IDENTIFIER: US 6329503 B1
TITLE: Serpentine transmembrane antigens expressed in human cancers and uses
thereof

---------- KWIC ---------

DEPR:
In another approach, a recently described sensitive assay for detecting and
characterizing carcinoma cells in blood may be used (Racila et al., 1998, Proc.
Natl. Acad. Sci. USA 95: 4589-4594). This assay combines immunomagnetic
enrichment with multiparameter flow cytometric and immunohistochemical
analyses, and is highly sensitive for the detection of cancer cells in blood,
reportedly capable of detecting one epithelial cell in 1 ml of peripheral
blood.

DOCUMENT-IDENTIFIER: US 5543296 A
TITLE: Detection of carcinoma metastases by nucleic acid amplification

---------- KWIC ---------

BSPR:
In another aspect of the present invention, carcinoma metastases in selected body tissues and fluids are detected by combining the advantages of immunocytology and nucleic acid amplification technologies. In this approach, monoclonal antibodies specific for carcinoma antigens that are not expressed by the malignant cells normally present in the selected body tissue or fluid are attached to immunomagnetic beads by standard methods (Lea et at., 1986, Scand. J. Immunol. 23:509, and Lea et al., 1988, J. Mol. Recogn. 1:9). The immunomagnetic beads are then incubated with cells obtained from the selected body tissue or fluid samples. Standard magnetic separations techniques as described in Lea et al., 1986, and 1989 supra., are used to enrich the sample for carcinoma cells expressing the target antigens. The separated magnetic beads and attached carcinoma cells are place in appropriate extraction buffers to isolate RNA. The extracted nucleic acids are then utilized in appropriate nucleic acid amplification assays to detect carcinoma associated mRNA.

BSPR:
Immunomagnetic enrichment of the tumor cell population enhances the sensitivity of nucleic acid amplification assays, by increasing the proportion of target nucleic acid sequences in the starting reaction mixture. In one embodiment of this enrichment method, useful for detecting lung carcinomas, commercially available magnetic beads are coated with sheep anti-mouse immunoglobulin (Dynabeads M450, Dynal Corporation) and incubated respectively with EA-1 (anti-NSCLC) and NCAM (anti-SCLC) specific monoclonal antibodies (10 .mu.g antibody per mg particle overnight at 4.degree. C). The antibody coated beads are then washed five times in phosphate buffered saline (PBS) containing 0.5% bovine serum albumin (BSA). The immunomagnetic beads are then suspended into 2 mils of BSA with 0.1% BSA and 0.01% NAN.sub.3. To detect carcinoma cells in

bone marrow of peripheral blood, ficoll-hypaque purified mononuclear cells from
bone marrow or peripheral blood specimens are mixed with the immunomagnetic
beads at a ratio of 1:10 in a T75 flask containing 25 mls of RMPI 1640 media
with 0.01% EDTA. The cells and immunomagnetic beads are incubated overnight on
a rocker platform at 4.degree. C. The flask is then place on a soft iron plate
with 10 samarium cobalt magnets for 5 minutes.

DOCUMENT-IDENTIFIER: US 5644033 A
TITLE: Monoclonal antibodies that define a unique antigen of human B cell
antigen receptor complex and methods of using same for diagnosis and treatment

---------- KWIC ---------

DEPR:
It is believed that B CLL, B PLL and HCL are closely related in the differentiation pathway of B cell ontogeny while non-T/non-B ALL derives from
normal counterparts at earlier stages of B cell ontogeny by malignant transformation and clonal expansion. B ALL is closely related to B lymphomas
(Magrath et al. "Bone marrow involvement in Burkitt's lymphoma and its relationship to acute B-cell leukemia" Leukemia Res., 4: 33, 1979) and its
phenotype corresponds to that of relatively mature B cells. B NHL consists of
a heterogeneous group of malignant B cells with varying degrees of maturation
but the normal counterparts in the majority of cases of B NHL appear to be
relatively mature B cells (Jaffe, "The role of immunophenotypic markers in the
classification of non-Hodgkin's lymphomas" Seminars Oncol., 17: 11, 1990).
Phenotypic and genetic analyses suggest that B PLL derives from normal counterparts by malignant transformation at a later developmental stage than B
CLL. For instance, B PLL cells express higher density of cell surface Ig than
B CLL cells. Furthermore, Luzzatto et al. reported that in most cases of B
PLL, the malignant clone has both alleles of Ig heavy chain gene in a rearranged configuration, while in many cases of B CLL, only one allele of the
gene is rearranged and the other is found in a germ line-like configuration
("DNA rearrangements of cell lineage specific genes in lymphoproliferative
disorders" Prog. Hematol., 14: 303, 1986). Similarly to B PLL, HCL also
appears to derive from the clonal expansion of a B cell at a later developmental stage than B CLL. Between HCL and B PLL, the normal counterparts
of HCL are probably more mature than those of B PLL in the differentiation
pathway of B cell ontogeny.

ORPL:
Jaffe "The role of immunophenotypic markers in the classification of non-Hodgkin's lymphomas" Seminars Oncol., 17: 11, 1990.

DOCUMENT-IDENTIFIER: US 5612185 A
TITLE: Method for identifying tumor cells in cell cycle arrest

---------- KWIC ---------

BSPR:
With reference to the treatment of B cell tumors, including non-Hodgkin's lymphoma, it is contemplated that antibodies directed against the cell surface Ig, and particularly against the idiotypic tumor marker Ig components, will be particularly useful as cell cycle arrest inducing components. Antibodies directed against Fc receptor and CD19-like molecules are also contemplated to be particularly useful in this regard.

DOCUMENT-IDENTIFIER: US 5304635 A
TITLE: Antigen specifically expressed on the surface of B cells and Hodgkin's
cells

---------- KWIC ---------

DEPR:
With regard to other antibodies employed in this study, we noted that L26, a
widely used pan-B cell marker, reacted with B cells in most cases of non-Hodgkin's lymphoma, thereby showing considerable overlap with anti-BLA-36.
However, L26 stained Reed-Sternberg cells and variants in only 5 of 16 cases of
Hodgkin's disease. The limited ability of L26 to stain Reed-Sternberg cells in
Hodgkin's disease, other than lymphocyte predominant type, is in agreement with
the experience of others (51). The failure of L26 to stain the Reed-Sternberg
cells and L&H cells in one of our cases of lymphocyte predominant Hodgkin's
disease is at variance with a report by Pinkus and Said (51) describing uniform
reactivity of L26 in this condition. A possible explanation for this discrepancy may related to accidental destruction of antigen during tissue
processing, since residual B cells in this case also were non-reactive for L26.

DOCUMENT-IDENTIFIER: US 5096810 A
TITLE: Monoclonal antibodies for diagnosis of hairy cell leukemia

---------- KWIC ---------

BSPR:
S-HCL-3 monoclonal antibody recognizes an antigen present on entirely different
cell lineages, namely macrophages of almost all tissues and polymorphonuclear
cells. This antigen is not expressed on any other malignant lymphocytes except
hairy cells. Moreover, this atnigen is not found on other non-Hodgkin
lymphomas which may resemble hairy cell leukemia (Neiman, R. S., Sullivan, A.
R., Jaffe, R. Cancer 43: 329 (1979)), and other Sig.sup.+ malignancies which
makes it a useful marker for distinguishing these malignancies for hairy all
leukemia.

PGPUB-DOCUMENT-NUMBER: 20010036459
DOCUMENT-IDENTIFIER: US 20010036459 A1
TITLE: Enhancement of antibody-mediated immune responses

---------- KWIC ---------

BSTX:
[0014] Well-defined tumor models for which therapeutic anti-tumor antibodies have been developed are known. For example, antibodies directed against the HER2/neu growth factor receptor prevent the growth of breast carcinoma cells in vitro and in vivo. Similarly, antibodies directed to the CD20 antigen on B cells arrests the growth of non-Hodgkin's lymphoma (Taji, H. et al., Jpn. J. Cancer Res., 1998, 89:748, which is incorporated herein by reference). These antibodies were developed based on their ability to interfere with tumor cell growth in vitro and are representative of a class which include those with specificities for the EGF receptor (Masul, H. et al., J. Cancer Res., 1986, 46:5592, which is incorporated herein by reference), IL-2R (Waldmann, T. A., Ann. Oncol., 1994,5 Supp.1: 13-7, which is incorporated herein by reference) and others (Tutt, A. L. et al., J. Immunol., 1998, 161:3176, which is incorporated herein by reference). Herceptin.RTM., a humanized antibody specific for the cellular proto-oncogene p185HER-2/neu (Pegram, M. D. et al., J. Clin. Oncol. 1998, 16:2659; Carter, P. et al., Proc. Natl. Acad. Sci. USA, 1992, 89:4285-4289, each of which is incorporated herein by reference), and Rituxan.RTM., a chimeric antibody specific for the B cell marker CD20 (Leget, G. A. and Czuczman, M. S., Curr. Opin. Oncol., 1998, 10:548-51, which is incorporated herein by reference), are approved for the treatment of HER-2 positive breast cancer and B cell lymphoma, respectively. A number of in vitro studies indicated that the critical mechanism responsible for the anti-tumor activities of Herceptin.RTM. and its mouse parent molecule 4D5 are due to receptor-ligand blockade (Kopreski, M. et al., Anticancer Res., 1996, 16:433-6; Lewis, G. D. et al., Cancer Immunol. Immunother., 1993, 37:255-63, each of which is incorporated herein by reference), while other in vitro

studies have
suggested that activities such as antibody dependent cellular
cytotoxicity
(ADCC) may be of importance (Carter, 1992, supra; Lewis, G. D. et al.,
Cancer
Immunol. Immunother., 1993, 37:255-63, which is incorporated herein by
reference). In vitro studies with Rituxan.RTM. and its murine parent
2B8 have
suggested a direct pro-apoptotic activity may be associated with this
antibody
(Shan, D. et al., Blood, 1998, 91:1644-52, which is incorporated herein
by
reference).

DOCUMENT-IDENTIFIER: US 6329503 B1
TITLE: Serpentine transmembrane antigens expressed in human cancers and uses
thereof

---------- KWIC ---------

BSPR:
The use of monoclonal antibodies to tumor-specific or over-expressed antigens
in the treatment of solid cancers is instructive. Although antibody therapy
has been well researched for some 20 years, only very recently have
corresponding pharmaceuticals materialized. One example is the humanized
anti-HER2/neu monoclonal antibody, Herceptin, recently approved for use in the
treatment of metastatic breast cancers overexpressing the HER2/neu receptor.
Another is the human/mouse chimeric anti-CD20/B cell lymphoma antibody,
Rituxan, approved for the treatment of non-Hodgkin's lymphoma. Several other
antibodies are being evaluated for the treatment of cancer in clinical trials
or in pre-clinical research, including a fully human IgG2 monoclonal antibody
specific for the epidermal growth factor receptor (Yang et al., 1999, Cancer
Res. 59: 1236). Evidently, antibody therapy is finally emerging from a long
embryonic phase. Nevertheless, there is still a very great need for new,
more-specific tumor antigens for the application of antibody and other
biological therapies. In addition, there is a corresponding need for tumor
antigens which may be useful as markers for antibody-based diagnostic and
imaging methods, hopefully leading to the development of earlier diagnosis and
greater prognostic precision.

DOCUMENT-IDENTIFIER: US 5480981 A
TITLE: CD30 ligand

---------- KWIC ---------

BSPR:
Hodgkin's Disease is a human lymphoma, the etiology of which is still not well understood. The neoplastic cells of Hodgkin's Disease are known as Hodgkin and Reed-Sternberg (H-RS) cells. CD30 is a 120 kd surface antigen widely used as a clinical marker for Hodgkin's lymphoma and related hematologic malignancies (Froese et al., J. Immunol. 139:2081 (1987); Pfreundschuh et al., Onkologie 12:30 (1989); Carde et al., Eur. J. Cancer 26:474 (1990)). Originally identified by the monoclonal antibody Ki-1, which is reactive with H-RS cells (Schwab et al., Nature (London) 299:65 (1982)), CD30 was subsequently shown to be expressed on a subset of non-Hodgkin's lymphomas (NHL), including Burkitt's lymphoma, as well as several virally-transformed lines (human T-Cell Lymphotrophic Virus I or II transformed T-cells, and Epstein-Barr Virus transformed B-cells (Stein et al., Blood 66:848 (1985); Andreesen et al., Blood 63:1299 (1984)). That CD30 plays a role in normal lymphoid interactions is suggested by its histological detection on a small population of lymphoid cells in reactive lymph nodes, and by induced expression on purified T- and B-cells following lectin activation (Stein et al., Int. J. Cancer 30:445 (1982) and Stein et al., 1985, supra).

DOCUMENT-IDENTIFIER: US 5407805 A
TITLE: Monoclonal antibody reactive to various human leukemia and lymphoma
cells and methods of using same for diagnosis and treatment

---------- KWIC ---------

DEPR:
In a separate experiment where detergent extracts of cell membranes of B CLL
cells were fractionated, SN7 antigen was found to bind to an LcH column. In
this experiment, therefore, HLL cell-membrane glycoprotein mixtures eluted from
an LcH column were used for immunoprecipitation after radiolabeling. Three
samples isolated from HLL cells derived from a CLL patient, another CLL patient
and two non-Hodgkin's lymphoma patients, respectively, were tested; the last
sample derived from a mixture of cells from two non-Hodgkin's lymphoma patients. The immunoprecipitates obtained by using the radiolabeled samples
and SN7 or an isotype-matching control mouse IgG (or control mAb) were analyzed
by SDS-PAGE and autoradiographs were prepared. These results are shown in FIG.
2 wherein immunoprecipitates from .sup.125 I-labeled cell membrane glycoprotein
mixtures were obtained from CLL patient a (left panel), CLL patient b (middle
panel) and non-Hodgkin's lymphoma patients (right panel). The
immunoprecipitation procedure used a 10-fold dilution of SN7 ascites (lanes A
and D of left panel, and lanes B and E of right panel), purified SN7 antibody
(lanes B and E of left panel, and lane B of middle panel), anti-HLA-DR mAb
(Becton Dickinson; lane A of middle panel, and lanes A and D of right panel)
and control mouse IgG (MOPC 195 variant; lanes C and F of left panel, lane C of
middle panel, and lanes C and F of right panel). The immunoprecipitates were
unreduced (lanes A, B and C of left and right panels) or reduced with
dithiothreitol (lanes D, E and F of left and right panels and lanes A, B and C
of middle panel) and analyzed by using 10% gels (left and middle panels) or 12%
gels (right panel). The marker proteins (shown in K daltons) were ovalbumin
(42.7), carbonic anhydrase (31.0), soybean trypsin inhibitor (21.5) and
lysozyme (14.4).

AU Foon K A

TI Laboratory and clinical applications of monoclonal antibodies for leukemias and **non-Hodgkin**'s lymphomas.

SO CURRENT PROBLEMS IN CANCER, (1989 Mar-Apr) 13 (2) 57-128. Ref: 376
Journal code: DU8; 7702986. ISSN: 0147-0272.

AN 89275839 MEDLINE

LA English

AB Important insights into leukocyte differentiation and the cellular origins of leukemia and lymphoma have been gained through the use of monoclonal antibodies that define cell surface antigens and molecular probes that identify immunoglobulin and T-cell receptor genes. Results of these studies have been combined with markers such as surface membrane and cytoplasmic immunoglobulin on B lymphocytes, sheep erythrocyte receptors on T lymphocytes, and cytochemical stains. After using all of the aforementioned markers, it is now clear that acute lymphoblastic leukemia (ALL) is heterogeneous. Furthermore, monoclonal antibodies that identify B cells, such as the anti-CD20 and anti-CD19 antibodies in combination with studies of immunoglobulin gene rearrangement, have demonstrated that virtually all cases of non-T-ALL are malignancies of B-cell origin. At least six distinct subgroups of non-T-ALL can now be identified. T-ALL is subdivided by the anti-CD7, anti-CD5, and antibodies that separate T lymphocytes subsets into three primary subgroups. Monoclonal antibodies are also useful in the subclassification of **non-Hodgkin**'s lymphoma, and certain distinct markers can be correlated with morphological classification. Although monoclonal antibodies are useful in distinguishing acute myeloid from acute lymphoid leukemias, they have less certain utility in the subclassification of acute myelogenous leukemia (AML). Attempts to subclassify AML by differentiation-associated antigens rather than by the French-American-British (FAB) classification are underway in order to document the potential **prognostic** utility of surface **markers**. Therapeutic trials using monoclonal antibodies in leukemia and lymphoma have been reported. Intravenous infusion of unlabeled antibodies is the most widely used method; transient responses have been demonstrated. Antibodies conjugated to radionuclides have been quite successful in localizing tumors of less than 1 cm in some studies. Therapy trials with antibodies conjugated to isotopes, toxins, and drugs have shown promise. Purging of autologous bone marrow with monoclonal antibodies and complement in vitro has been used in ALL and **non-Hodgkin**'s lymphoma; preliminary data suggest that this approach may be an effective therapy and may circumvent many of the obstacles and toxicities associated with in vivo monoclonal antibody infusion.

AU Harris N L
TI Lymphoma 1987. An interim approach to diagnosis and classification.
SO PATHOLOGY ANNUAL, (1987) 22 Pt 2 1-67. Ref: 141
Journal code: OS2; 0050610. ISSN: 0079-0184.
AN 88067316 MEDLINE
LA English
AB When immunophenotyping is used for diagnosis, it is essential to use panels of antibodies, rather than a single marker for a specific tumor type. There is virtually no single **marker** that is absolutely **diagnostic** and completely reliable for any particular neoplasm. For the most important clinical differential diagnoses--reactive versus neoplastic lymphoid lesions and lymphoma versus nonlymphoid tumor--relatively simple panels of antibodies are usually sufficient. In the former situation, immunoglobulin heavy and light chains (G, M, kappa, lambda) and a pan-T-cell antibody (Leu-4) will usually provide the answer. For the latter circumstance, kappa and lambda, a pan-leukocyte antibody, a pan-B-cell (B1), and a pan-T-cell antibody (Leu-4) along with cytokeratin constitute the initial panel. Further subclassification of lymphomas and leukemias can proceed using other antibodies as indicated in the preceding specific sections on the lymphomas. The use of specific antibodies for nonlymphoid tumors will be dictated by the morphologic appearance of the tumor. These may be used as a second panel if the initial screening does not establish a diagnosis of lymphoma. Performing and interpreting immunohistologic studies requires experience, and probably should not be attempted by laboratories that do not encounter a large number of lymphomas. Frozen tissue can be obtained and stored at -20 degrees for a few days; if immunohistologic studies are deemed necessary, the frozen tissue can be sent on dry ice to a reference laboratory. In preparing biopsy specimens for immunohistologic studies, and in interpreting the results of these studies, it is necessary to bear in mind the fact that morphology remains the most important tool for the diagnosis and subclassification of hematologic neoplasms. Obtaining tissue for marker studies should not be permitted to interfere with adequate morphologic examination. Similarly, artifacts and technical problems can occasionally lead to misleading results; the immunohistologic studies must be interpreted in light of the case as a whole, and should never be allowed to contradict common sense.

L Number	Hits	Search Text	DB	Time stamp
1	557	immuno$1mag$3ic or immuno$1bead$1	USPAT; US-PGPUB	2002/04/03 14:00
2	1516	non$1ho$4in$3	USPAT; US-PGPUB	2002/04/03 14:01
3	2	(immuno$1mag$3ic or immuno$1bead$1) same non$1ho$4in$3	USPAT; US-PGPUB	2002/04/03 14:02
4	8713	lymphoma or nhl	USPAT; US-PGPUB	2002/04/03 14:02
5	12	(immuno$1mag$3ic or immuno$1bead$1) same (lymphoma or nhl)	USPAT; US-PGPUB	2002/04/03 14:08
6	124	(immuno$1mag$3ic or immuno$1bead$1) same enrich$	USPAT; US-PGPUB	2002/04/03 14:08
7	124	(immuno$1mag$3ic or immuno$1bead$1) same enrich$6	USPAT; US-PGPUB	2002/04/03 14:13
8	768987	detect$5 or diagnos$5	USPAT; US-PGPUB	2002/04/03 14:14
9	30	((immuno$1mag$3ic or immuno$1bead$1) same enrich$) same (detect$5 or diagnos$5)	USPAT; US-PGPUB	2002/04/03 14:21
10	385265	cell or lym$4cyte$1	USPAT; US-PGPUB	2002/04/03 14:22
11	23	(((immuno$1mag$3ic or immuno$1bead$1) same enrich$) same (detect$5 or diagnos$5)) same (cell or lym$4cyte$1)	USPAT; US-PGPUB	2002/04/03 14:22
-	1828	non$2ho$4in$3	USPAT; US-PGPUB	2002/04/03 13:59
-	1516	non$1ho$4in$3	USPAT; US-PGPUB	2002/04/03 14:01
-	70331	marker	USPAT; US-PGPUB	2002/04/03 12:31
-	11	non$1ho$4in$3 with marker	USPAT; US-PGPUB	2002/04/03 12:10
-	58012	anti$1bod$4	USPAT; US-PGPUB	2002/04/03 12:32
-	19	non$1ho$4in$3 same marker same anti$1bod$4	USPAT; US-PGPUB	2002/04/03 12:37
-	14	(non$1ho$4in$3 same marker same anti$1bod$4) not (non$1ho$4in$3 with marker)	USPAT; US-PGPUB	2002/04/03 12:38

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=> d his;log hold

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     FILE 'MEDLINE' ENTERED AT 12:41:26 ON 03 APR 2002
               E NON HODGKINS/CT
               E E2+ALL/CT
               E E14+ALL
L1         26036 S (NON HODGKIN?) OR NONHODGKIN?
L2          8616 S (PROGNOS? OR DIAGNOS?)(4A)MARKER#
L3           142 S L1 AND L2

     FILE 'STNGUIDE' ENTERED AT 12:50:34 ON 03 APR 2002
L4             0 S ENRICH?(15A)L1

     FILE 'MEDLINE' ENTERED AT 13:19:02 ON 03 APR 2002
L5             9 S ENRICH?(15A)L1

     FILE 'STNGUIDE' ENTERED AT 13:19:20 ON 03 APR 2002

     FILE 'MEDLINE' ENTERED AT 13:27:19 ON 03 APR 2002
L6         85522 S IMMUNOMAGNETIC OR IMMUNOBEAD CELL SORTING OR SEPARATION
L7         27820 S IMMUNOMAGNETIC OR IMMUNOBEAD# OR (CELL#(3A)(SORTING OR SEPARA
L8            13 S L1(15A)L7
L9            12 S L8 NOT L5

     FILE 'STNGUIDE' ENTERED AT 13:30:19 ON 03 APR 2002

                                                    SINCE FILE      TOTAL
COST IN U.S. DOLLARS                                   ENTRY     SESSION
                                                        0.54       25.38
FULL ESTIMATED COST

 SESSION WILL BE HELD FOR 60 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 13:35:43 ON 03 APR 2002
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L Number	Hits	Search Text	DB	Time stamp
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2	1516	non$1ho$4in$3	USPAT; US-PGPUB	2002/04/03 12:09
3	70331	marker	USPAT; US-PGPUB	2002/04/03 12:31
4	11	non$1ho$4in$3 with marker	USPAT; US-PGPUB	2002/04/03 12:10
5	58012	anti$1bod$4	USPAT; US-PGPUB	2002/04/03 12:32
6	19	non$1ho$4in$3 same marker same anti$1bod$4	USPAT; US-PGPUB	2002/04/03 12:37
7	14	(non$1ho$4in$3 same marker same anti$1bod$4) not (non$1ho$4in$3 with marker)	USPAT; US-PGPUB	2002/04/03 12:38